Chromosome Conformation in Context

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Chromosome conformation capture (3C) techniques have revealed many features about the structure of chromatin: Large scale organization into two compartments (A and B), relatively stable partitioning into Topologically Associating Domains (TADs) at the megabase scale, and more dynamic and cell type specific interactions associated with various architectural proteins at the sub-megabase scale (sub-TADs). However, these assays are limited in that they only interrogate interactions between chromatin without any connection to location in the nucleus, and are an ensemble measurement over thousands of cells. Here we use integrated analysis of chromosome conformation capture (Hi-C) data, DamID, and single cell imaging to understand the relationship of chromosome conformation features with a specific nuclear compartment, the periphery. Using a new high-resolution compartment scoring algorithm, we show that the B (or generally less active) compartment corresponds to Lamin Associated Domains (LADs) which are positioned at the nuclear lamina. These regions have a histone modification profile typical of heterochromatin, but are also depleted of the architectural protein CTCF suggesting their organization is CTCF independent. However within the LADs we find many small regions (less than 25kb) that have low signal for Lamin association and a dramatic change in compartment score. These regions are highly enriched for histone states and DNA binding proteins associated with active elements, and appear to contain both transcription start sites and a large number of putative *cis*-regulatory modules. This suggests regions much smaller than a stereotypical TAD can be organized into a different nuclear compartment from their surrounding DNA, and that this organization is involved in gene regulation at a distance.